UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,505	04/06/2001	Eyal Raz	UCAL-203	6822

24353 7590 07/15/2005

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,505	RAZ ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7,10,14,20,21,27,28,30-35,37-45 and 47-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3,4,7,34,35,37 and 38* is/are allowed.

6)☒ Claim(s) *10,14,20,21,27,30-33,39-45 and 47-50* is/are rejected.

7)☒ Claim(s) *28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed on 4/15/05 has been entered.

Amended claims 3-4, 7, 10, 14, 20-21, 27-28, 30-35, 37-45 and 47-50 are pending in the present application, and they are examined on the merits herein.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn in light of Applicants' amendment.

The art rejections in the Office action mailed on 6/2/04 are withdrawn in light of Applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 is indefinite because it is dependent on canceled claim 36. Accordingly, the metes and bounds of the claim are not clearly determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 10, 27, 33 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Dow et al. (US 6,693,086). ***This is a new ground of rejection necessitated by Applicants' amendment.***

Dow et al disclose a method and composition to elicit a systemic immune response against allergic inflammation in a mammal (e.g., humans, dogs, cats, mice, rats, preferably humans), specifically an enhanced Th1-type response that results in reduced or alleviated allergic inflammation (col. 3, lines 16-48; col. 5, lines 3-22; col. 6, lines 59-62; and particularly col. 36, lines 22-60). A disease associated with allergic inflammation is a disease in which the elicitation of one type of immune response, e.g., a Th2-type immune response, against a sensitizing agent and the Th2-type immune response is characterized by the predominant production of IgE whereas a Th1-type

immune response is characterized sometimes by the production of an IgG2a or an IgG3 antibody isotype (col. 15, lines 4-20; col. 36, lines 26-33). The composition comprises a recombinant nucleic acid encoding an allergen that is operatively linked to a transcription control sequence, wherein the allergen includes plant pollens (col. 5, line 5), and the allergen encoding nucleic acid can be obtained from its natural source, either as an entire gene or a portion thereof that encodes epitopes that are recognized by T cells and B cells (col. 18, lines 13-31; col. 20, lines 27-37). Dow et al also teach that the recombinant nucleic acid contains secretory signals to enable an expressed immunogen or allergen from the cell that produces the protein, and suitable signal segments include a cytokine signal segment as well as any heterologous signal segment capable of directing the secretion of an immunogen (col. 22, lines 48-62). It is further noted that Dow et al disclose various mammalian cytokine nucleic acid molecules (col. 21, lines 8-24). Dow et al further teach that the recombinant nucleic acid can be modified to correspond to the codon usage of the host cell, with human is a preferred mammal, indicating that the plant pollen allergen encoding nucleic acid can contains analogous human codons (col. 23, line 66 continues to line 1 of col. 24). Moreover, Dow et al teach that the nucleic acid molecule can also be modified to make nucleic acids more immunostimulatory, such as by the addition of CpG moieties to the nucleic acids (col. 28, lines 5-9).

The teachings of Dows et al meet all the limitation of the instant claims. Accordingly, the reference anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10, 14, 27, 30, 39 and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (US 6,693,086) in view of Rogers et al. (U.S. 5,776,761; Cited previously). ***With respect to claim 39, this constitutes a new ground of rejection.***

Dow et al disclose a method and composition to elicit a systemic immune response against allergic inflammation in a mammal (e.g., humans, dogs, cats, mice, rats, preferably humans), specifically an enhanced Th1-type response that results in reduced or alleviated allergic inflammation (col. 3, lines 16-48; col. 5, lines 3-22; col. 6, lines 59-62; and particularly col. 36, lines 22-60). A disease associated with allergic

inflammation is a disease in which the elicitation of one type of immune response, e.g., a Th2-type immune response, against a sensitizing agent and the Th2-type immune response is characterized by the predominant production of IgE whereas a Th1-type immune response is characterized sometimes by the production of an IgG2a or an IgG3 antibody isotype (col. 15, lines 4-20; col. 36, lines 26-33). The composition comprises a recombinant nucleic acid encoding an allergen that is operatively linked to a transcription control sequence, wherein the allergen includes plant pollens (col. 5, line 5), and the allergen encoding nucleic acid can be obtained from its natural source, either as an entire gene or a portion thereof that encodes epitopes that are recognized by T cells and B cells (col. 18, lines 13-31; col. 20, lines 27-37). Dow et al also teach that the recombinant nucleic acid contains secretory signals to enable an expressed immunogen or allergen from the cell that produces the protein, and suitable signal segments include a cytokine signal segment as well as any heterologous signal segment capable of directing the secretion of an immunogen (col. 22, lines 48-62). It is further noted that Dow et al disclose various mammalian cytokine nucleic acid molecules (col. 21, lines 8-24). Dow et al further teach that the recombinant nucleic acid can be modified to correspond to the codon usage of the host cell, with human is a preferred mammal, indicating that the plant pollen allergen encoding nucleic acid can contains analogous human codons (col. 23, line 66 continues to line 1 of col. 24). Moreover, Dow et al teach that the nucleic acid molecule can also be modified to make nucleic acids more immunostimulatory, such as by the addition of CpG moieties to the nucleic acids (col. 28, lines 5-9).

Dow et al do not specifically teach methods and compositions containing a ragweed encoding nucleic acid molecule, and specifically the Amb a1 ragweed encoding nucleic acid molecule.

At the effective filing date of the present application, Rogers et al already disclose cDNAs encoding Amb al allergic proteins or peptides (see at least the abstract). Additionally, Rogers et al teach that Amb a1 is the major allergenic component of short ragweed pollen and the major cause of late summer hayfever in North America and Canada (col. 1, lines 51-56; col. 2, lines 12-15).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the methods and compositions of Dow et al by utilizing nucleic acids encoding Amb a1 allergic proteins or peptides taught by Rogers et al. to desensitize a mammal with allergic inflammation associated with hayfever.

One of ordinary skilled artisan would have been motivated to carry out the above modification because Amb a1 is the major allergenic component of short ragweed pollen and the major cause of late summer hayfever in North America and Canada.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Dow et al., Rogers et al., coupled with a high level of skill possessed by an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 10, 14 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (US 6,693,086) in view of Singh et al. (U.S. Patent No 5,965,455; Cited previously). ***This is a new ground of rejection necessitated by Applicants' amendment.***

The teachings of Dow et al have been presented above. However, Dow et al do not specifically teach methods and compositions containing a grass pollen encoding nucleic acid molecule.

However, at the effective filing date of the present application, Singh et al. already disclose nucleic acid sequences coding for two ryegrass pollen allergen Lol p Ib family members, and fragments (see at least the abstract). Moreover, Singh et al teach that allergens constitute the most abundant proteins of grass pollen, which is the major cause of allergic disease in temperate climates (col. 1, lines 62-64).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the methods and compositions of Dow et al by utilizing nucleic acids encoding ryegrass pollen allergens taught by Singh et al. to desensitize a mammal with an allergic disease.

One of ordinary skilled artisan would have been motivated to carry out the above modification because grass pollen is the major cause of allergic disease in temperate climates as taught by Singh et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Dow et al., Singh et al., coupled with a high level of skill possessed by an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 10, 20-21, 27, 31-32, 41, 44-45 and 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (US 6,693,086) in view of Carson et al. (WO 98/16247, IDS). ***This is a new ground of rejection necessitated by Applicants' amendment.***

The teachings of Dow et al have been presented above. However, Dow et al do not specifically teach methods and compositions containing an immunostimulatory nucleotide sequence (ISS) comprising the sequence AACGTT or at least one phosphorothioate backbone or further comprising a universal antigen or an immunogenic fragment thereof.

However, at the effective filing date of the present application Carson et al. already disclosed various CpG motifs, including those recited by the instant claims (page 4, lines 18-23; page 15, line 20 continues to line 17 of page 16) that are useful for the induction of Th1-type immune responses. Carson et al also teach the CpG immunostimulatory polynucleotide (ISS-PN) can also contain phosphorous and non-phosphorous based modified oligonucleotides including phosphorothioates (page 21, line 17 continues to line23 of page 22). Carson et al further teach that other useful adjuvants to be include in the immunomodulatory compositions include cholera toxin, cholera toxin B subunit, fungal polypeptides, non-Helicobacter pylori bacterial lysates, labile toxin of *E.Coli* and others (page 20, lines 19-23), and some of these would

constitute or fall within the scope of a universal antigen or an immunogenic fragment thereof.

Accordingly, it would have been obvious for an ordinary skilled artisan to use the compositions comprising CpG motifs containing oligonucleotides as well as other useful adjuvants taught by Carson et al. in the methods and compositions disclosed by Dow et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because the compositions comprising CpG motifs containing oligonucleotides as well as other useful adjuvants taught by Carson et al. have been shown to be useful for the induction of Th1 responses that are beneficial for treating allergies.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Dow et al. and Carson et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

Claims 3-4, 7, 34-35 and 37-38 are allowed.

Claim 28 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art of record does not teach or fairly suggest a polynucleotide composition comprising a nucleic acid sequence encoding a plant allergen, wherein the nucleic acid encoding the plant allergen is further modified to include a nucleic acid encoding a signal sequence comprising specifically a hemagglutinin signal sequence that is operatively linked to the allergen-encoding nucleic acid, and a method of using the same.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Quang Nguyen, Ph.D.

DAVID GUZO
PRIMARY EXAMINER